JPPT | Case Report

# Ivabradine Monotherapy for the Treatment of Congenital Junctional Ectopic Tachycardia in a Premature Neonate

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Congenital junctional ectopic tachycardia is a rare and special type of supraventricular arrhythmia. Junctional ectopic tachycardia is characterized by persistently elevated heart rates that may cause an impairment in cardiac function. Junctional ectopic tachycardia is considered one of the most difficult-to-treat conditions even with a combination of antiarrhythmic medications. Ivabradine is a novel antiarrhythmic medication used to decrease the heart rate in adults with angina pectoris. We report a first case of a premature neonate with a normal heart structure who developed junctional ectopic tachycardia and was subsequently treated successfully with ivabradine.

**ABBREVIATIONS** ECG, electrocardiogram; ECHO, echocardiogram; FDA, US Food and Drug Administration; JET, junctional ectopic tachycardia; QRS, ECG indication of ventricular contraction from the Q, R, and S waves

**KEYWORDS** case report; congenital; ivabradine; junctional ectopic tachycardia; premature neonate

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## Introduction

Congenital junctional ectopic tachycardia (JET) is rare and is considered one of the most difficult cardiac arrhythmias to manage.[1] The morbidity and mortality of infants with JET have been high, especially if it is non-post-operative congenital JET.[1,2] Ivabradine is a novel cardiac pacemaker cell inhibitor, bradycardic agent with a specific mechanism of action that is related to selective inhibition of hyperpolarization-activated cyclic nucleotide-gated channels, subsequently reducing heart rate.[3] It revealed its efficacy in reducing heart rate and improving the outcome of patients with chronic heart failure.[4] Limited studies showed that demonstration of ivabradine in a pediatric population has a promising outcome. However, none of these studies were on premature neonates with a weight less than 2 kg.[5-7]

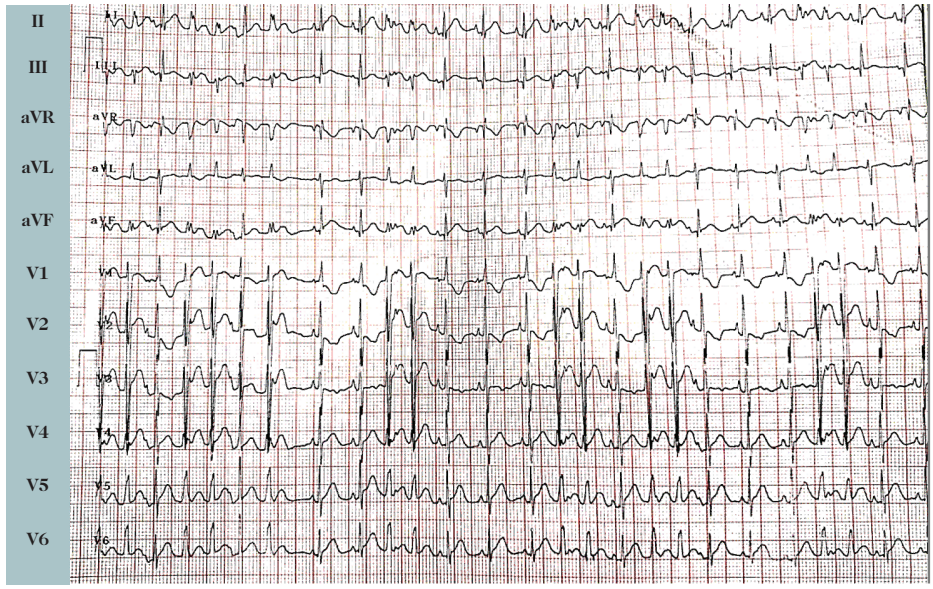
We present a case of hemodynamically stable premature neonate with a normal heart structure who presented with congenital JET at the age of 19 days. Following unsuccessful trials in treating patients with JET symptoms using amiodarone infusion and propranolol, we were able to control the patient's symptoms using ivabradine only.

## Case Report

A male with birth weight of 1800 g was born at 31 weeks' gestation and was delivered by emergency cesarean delivery with Apgar scores of 6 and 9 at 1 and 5 minutes, respectively. The neonate was admitted to the neonatal intensive care unit because of respiratory distress syndrome, was intubated, and was given 1 dose of a surfactant. Ampicillin and amikacin were administered through a peripheral line as empiric therapy for early neonatal sepsis. Fetal ultrasound showed a suspicion of congenital heart disease; hence, a transthoracic echocardiogram (ECHO) was performed on the second day of life. The ECHO revealed a small atrial septal defect secundum and moderate patent ductus arteriosus (1.7 mm) with a left-to-right shunt. The heart anatomy and function were normal. At the age of 19 days, the neonate started to develop an unexplained tachycardia with a heart rate between 190 and 220 bpm. A second ECHO showed normal anatomy of the heart and complete premature ventricular contraction. Thus, a 12-lead ECG was performed and revealed a narrow QRS and atrioventricular-dissociated supraventricular tachycardia with ventricular rate ranges between 170 and 280 bpm and atrial rate at 150 bpm (Figure 1). Our patient did not have any central venous catheter placement.

Propranolol was started with a dosage of 0.25 mg/kg/dose orally every 12 hours. After 2 days, a Holter monitor showed supraventricular tachycardia in the forms of JET with a frequent attack. Therefore, continuous intravenous infusion of amiodarone (10 mcg/kg/min) was started, and propranolol was gradually increased up to 1 mg/kg/dose orally every 6 hours. Despite these therapies, ECG continued to show JET with a heart rate between 250 and 290 bpm. On day 26 of life, ivabradine (Corlanor, Servier Laboratories, Hawthorn, Australia) was started (i.e., 0.05 mg/kg/dose orally every 12 hours), and propranolol and amiodarone were continued. On the following day, the 24 hours of Holter monitoring showed a sinus rhythm with intermittent

**Figure 1.** Electrocardiogram revealed a narrow QRS and AV-dissociated supraventricular tachycardia with ventricular rate ranges between 170-280 bpm and atrial rate at 150 bpm.




JET. After 3 days of ivabradine, the Holter monitoring revealed sinus rhythm.

By the second week of ivabradine, the neonate developed bradycardia; thus, amiodarone and propranolol were tapered and discontinued, and the dosage of ivabradine was decreased to 0.04 mg/kg/dose orally every 12 hours. The average heart rate on the patient's Holter monitor prior to discharge was 100 to 120 bpm (Figure 2). The patient was discharged at 38 weeks of age (2.48 kg) on 0.08 mg/kg/day ivabradine in 2 divided doses (1 mL per dose). Junctional ectopic tachycardia recurrence was not noticed within the following 6 months.

## Discussion

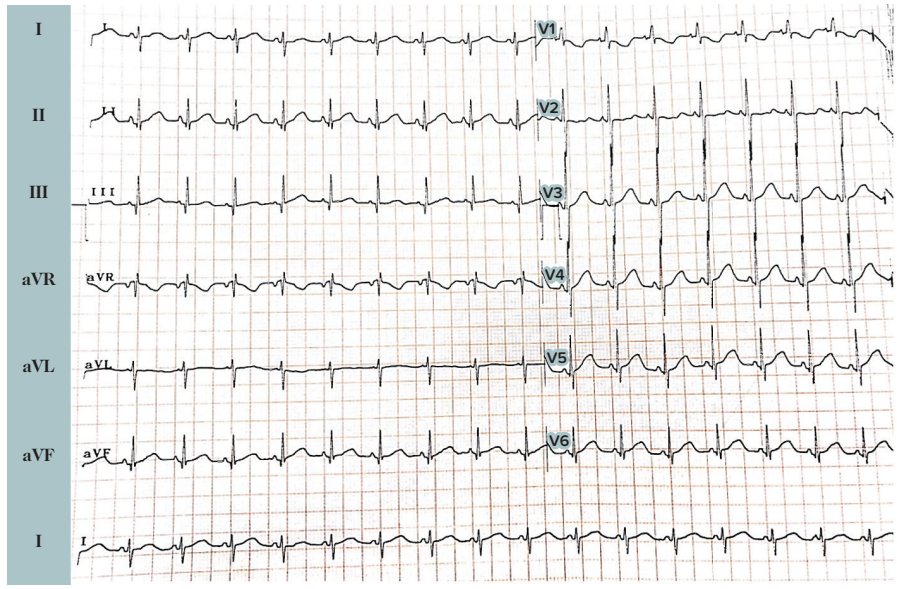
We report the use of ivabradine as monotherapy in a preterm neonate with congenital JET associated with a structurally normal heart and a hemodynamically stable case. Junctional ectopic tachycardia is an arrythmia that can be divided into congenital idiopathic (non-post-operative JET) or transient JET due to post-operation of congenital heart disease.[1] Not only is congenital JET rare, it is difficult to treat, especially if it occurs before the first 6 months of age.[1,8] These patients also have a high risk of adverse outcomes, including cardiomyopathy and sudden death.[1,9] The mortality rate was 4% for pediatric non-post-operative JET.[1] The mechanism of the tachycardia is thought to be abnormal automaticity arising from the region of the atrioventricular node proximal bundle of His.[3] A non-pharmacologic approach using radiofrequency ablation or cryoablation may provide a complete cure in older patients[1,2]; however, in infants pharmacologic therapy with amiodarone alone or in combination with beta-blockers, digoxin, and flecainide is considered to be first-line therapy.[1,2,8]

Ivabradine, a new-generation antiarrhythmic, selectively inhibits the spontaneous pacemaker activity of the sinus node by blocking the cardiac pacemaker I(f) current.[10] Ivabradine is routinely used in adults to lower heart rate in angina and heart failure[10] and is FDA approved for the management of heart failure in adults. Although it is not FDA labeled for use in pediatric patients, its use in a few pediatric and infant cases have been reported.[11-14]

The first case involved a term neonate with a birth weight of 3.5 kg, and the second case occurred in a premature neonate with a birth weight of 2.17 kg.[11] Both cases developed hemodynamically unstable JET and cardiopulmonary resuscitation done immediately after birth.[11] Furthermore, the preterm neonate developed JET due to a structurally abnormal heart with hypertrophic cardiomyopathy and mild valvular pulmonary stenosis.[11]

Unlike the premature neonate reported by Jana-Katharina,[11] our patient developed JET at 19 days of life. Moreover, our neonate had a structurally normal heart, was hemodynamically stable, and did not receive inotropes during the length of hospital stay. Furthermore, there is a little information regarding the use of ivabradine in a neonate with low birth weight (1.8 kg), much less the successful use of ivabradine as monotherapy in the treatment of congenital JET in neonates and infants. Ivabradine was used at 0.05 to 0.1 mg/kg/

**Figure 2.** Electrocardiogram showed a sinus rhythm after initiation of ivabradine with average heart rate 100 bpm.




day in 2 divided doses in 1 study.[6] In a different study the doses were increased up to 0.28 mg/kg/day.[11] Our patient initially received 0.1 mg/kg/day. Later and because of a decrease in heart rate between 60 and 85 bpm, we reduced the dosage to 0.08 mg/kg/day with no significant adverse effect noted. Ivabradine is metabolized by hepatic cytochrome 3A4 enzyme CYP3A4.[14] The activity of this isozyme in premature neonates is as low as 30% to 40% in comparison with adult activity.[15,16] The neonate also received amiodarone, which is a moderate inhibitor of CYP3A4.[15,16] For these 2 reasons, the serum ivabradine concentration in premature neonates is expected to be higher than that in adults.[15,16]

There are some limitations to our study. The first and most important one is that it represents a single case report. Second, although ivabradine can cause bradycardia, we assumed propranolol and amiodarone or a combination of all three is the cause for our patient's bradycardia. We decreased and stopped propranolol and amiodarone, and consequently the bradycardia resolved. Third, ivabradine was administered orally using an extemporaneously compounded product. Our patient was hemodynamically stable. However, in some cases where patients could experience sequences of severe tachycardia, the intravenous formulation should be available. Fourth, ivabradine was not used as first-line therapy in our case. Finally, we could not assess the long-term efficacy and safety of ivabradine in neonate. Our study describes the successful use of low-dose ivabradine in controlling the JET in a premature neonate weighing <2 kg.

## Conclusion

Ivabradine monotherapy was effective in controlling the JET in a premature neonate weighing <2 kg with a dosage <0.1 mg/kg/day. We suggest using ivabradine after failed beta-blockers and other cardiac antiarrhythmic medications, such as amiodarone, and using it under cardiac team monitoring. Further investigations and clinical studies are warranted to determine the appropriate dose and adverse reactions of ivabradine in neonates.

### Article Information

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review was not required and informed consent was not obtained.

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